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Prognostication of Acute Myeloid Leukemia Needs Incorporation of CD25 Status

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Interleukin-2 receptor (IL-2R) is composed of three different subunits (α, β, γ chain). CD25 is known as the IL-2Rα chain, and has been proved to be expressed not only on normal lymphocytes but also on various kinds of acute and chronic leukemia cells [1]. In 1992, we first reported the prognostic importance of CD25 expression on leukemia cells from Japanese adult patients with acute myeloid leukemia (AML) [2]. During the past three decades, several cell surface antigens have been described to be as poor prognostic predictors in AML patients [3]. Currently, cytogenetics at diagnosis has become the most powerful prognostic indicator in AML, and is widely adopted to stratify AML patients into three discrete categories as follows: the favorable-prognosis, intermediate-prognosis, and adverse-prognosis groups [4]. However, more than half of AML patients are allocated to the intermediate-risk category, and this group is thought to be biologically heterogenous and prognostically further distinguishable [5-8]. Although the prognostic relevance of cell surface markers appear to be controversial for the time being, only CD25 has recently been reevaluated as an independent strong adverse predictor and such reports have been published in a row in western countries [5-7]. Their and our recent data [8] have indicated that by incorporating the CD25 status in the cytogenetic classification, a significant high-risk cohort equivalent to the adverse-risk category was sorted out from the subset with intermediate-risk cytogenetics. On the other hand, gene-mutation and gene-expression studies have also identified numerous molecular markers carrying prognostic value in patients with AML. Among them, internal tandem duplication of FLT3 (FLT3-ITD) has been shown by many studies to be the most important genetic indicator which predicts inferior clinical outcome [9]. Interestingly, the presence of FLT3-ITD is described to be uniformly related to CD25 expression probably because FLT3-ITD directly triggers the constitutive activation of STAT5, which is an established CD25 transcription factor [5,6]. On the other hand, CD25 expression is dependent not only on STAT5 but also on other factors and additional mechanisms including methylation pattern of CD25 gene promoter. In fact, aberrant expression of CD25 has been identified in up to approximately 60-70% of FLT3-ITD (+) AML cases [5,7]. Of note, the adverse prognostic impact of FLT3-ITD is demonstrated to be restricted to CD25 (+) cases [6]. Therefore, CD25 expression is now considered to be one of the most important prognostic biomarkers in AML independent of both cytogenetic and genetic aberrations. Practically, molecular insights have not become manifest in routine clinical use, and are not available for all patients. Unsuccessful karyotyping is also experienced sometimes. In contrast, CD25 testing is easily carried out by flow cytometric immunophenotyping using a monoclonal antibody against CD25, and it is cost-effective and less time-consuming. In addition, some studies have indicated that CD25 expression is highly identified in leukemic stem cells [6], and is significantly associated with the incidence of minimal residual disease after chemotherapy [5], which also support the prognostic relevance of CD25 expression in AML. Recently, it has been reported that even allogeneic hematopoietic stem cell transplantation shows only a limited effect on CD25 (+) AML [10]. However, at present CD25 status has not yet obtained a citizenship officially as one of the useful prognostic biomarkers in the field of AML risk assessment. We strongly propose that CD25 survey should be integrated into current prognosis predicting system in AML as soon as possible to improve further AML prognostication. Recognition of CD25 (+) AML is also essential for better understanding of its biological characteristics and the development of an effective treatment strategy for this poor prognostic disease.

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